



COMMENTARY

Adverse-Event Reports in Over-the-Counter Topical Acne Drug Products Containing Benzoyl Peroxide from a Specific Pharmaceutical Company in the USA

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ABSTRACT

Benzoyl peroxide (BPO) has been used extensively in dermatology, often for the treatment of acne vulgaris. In a 20-year period, dermatologists in the United States used over-the-counter BPO more than 13 million times. However, skin irritation and other adverse events (AEs) are associated with the use of BPO. AEs associated with BPO were identified using the Galderma pharmacovigilance system, which collects AE reports from multiple sources. Over approximately 20 years, 558 AE reports were collected from the database, ranging from application site reactions to systemic hypersensitivity reactions, resulting in a reporting rate of under 1%. These data show that the risk of OTC topical acne drug products containing BPO is low.

Keywords: BPO; Benzoyl peroxide; Topical; Acne; Rosacea; Tolerability

Key Summary Points

Why carry out this study?

Benzoyl peroxide (BPO) has been used extensively in dermatology over the last 60 years, and over a 20-year period was recommended for use by dermatologists over 13 million times.

A common adverse event (AE) associated with BPO use is skin irritation.

The goal of this study was to determine the number and type of reported AEs associated with use of BPO through a pharmacovigilance system.

What was learned from the study?

The search identified 558 adverse events reports, of which one was assessed to have had a serious outcome while 557 were assessed to have had nonserious outcomes, and the ten most commonly reported AEs made up 66% of all reported AEs.

The reporting rate of AE reports concerning the use of over-the-counter (OTC) topical acne drug products containing BPO appears to be approximately 0.014%.

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Given this very low rate of AE reports, the risk–benefit of OTC topical acne drug products containing BPO is considered to be positive.

INTRODUCTION

First approved in 1960 for the treatment of acne [1], benzoyl peroxide (BPO) is used in prescription and over-the-counter (OTC) products as cream, gel, lotion, foam, and cleanser formulations in concentrations from 2.5 to 10% [2–4].

Over the past 60 years, BPO has been used extensively in dermatology, accounting for more than 13 million OTC usages by dermatology healthcare providers in the US between 1989 and 2008 alone, second only to OTC hydrocortisone [5].

The most common adverse event (AE) associated with BPO use is skin irritation, which occurs more frequently at higher concentrations and tends to lessen with continued use [2, 6, 7].

This commentary discusses almost three decades of AE reports concerning the use of OTC topical acne drug products containing BPO.

ADVERSE EVENT REPORTS

The Galderma pharmacovigilance system receives spontaneous AE reports from consumers, physicians, market research, literature, and various other sources. This allows identification of previously unknown AEs, changes in the frequency or severity of known AEs, and assessment of a drug's benefit–risk to determine if action is required to improve the drug's benefit–risk.

A search for AE reports concerning the use of prescription and OTC topical acne drug products containing only BPO as the active ingredient was conducted using the Galderma Global Safety Database covering the following time interval: 1992 through October 15, 2021. The search identified 558 AE reports in the United States during this time period. Due to increased

Box 1 AEs reported in the one case with a serious outcome

Pharyngitis	Hypoxia
Cough	Dyspnea
Pyrexia	Pleural effusion
Nausea	Pneumothorax
Vomiting	Respiratory failure
Dizziness	Pneumomediastinum
Viral infection	Jugular vein thrombosis

monitoring by Galderma of OTC BPO, most AEs were reported after 2018.

Of the 558 reported cases, one was assessed to have had a serious outcome while 557 were assessed to have had nonserious outcomes. No fatalities were reported. The one reported case with a serious outcome came from a published literature article [8]. The patient was hospitalized with life-threatening, medically significant events (Box 1). All reported events were unlisted and assessed medically to be unlikely related. At the time of the report, the patient was recovering, and it was unknown if the patient discontinued the drug, however, all events were medically assessed to be unlikely related to OTC topical acne drug products containing BPO.

Approximately 62% ($n = 347$) of the patients were female and the average patient age was 28 years (range, 7–78 years). Sixty-six percent ($n = 368$) of cases were reported without an age or age group being specified; however, for the remaining cases, reported AEs occurred in all age groups: 23% in adults ($n = 131$), 8% in adolescents ($n = 47$), 1% in children ($n = 1$), and 1% in elderly patients ($n = 5$).

Reported AEs ranged from application site reactions (e.g., skin irritation, burning sensation, erythema, dermatitis) to systemic hypersensitivity reactions (e.g., shortness of breath, swelling of the eyes, lips, or face). The ten most commonly reported AEs made up 66% of all reported AEs and included dry skin (15%, $n = 226$), skin burning sensation (9%, $n = 132$), erythema (8%, $n = 114$), drug ineffectiveness (8%, $n = 114$), acne (6%, $n = 92$), skin irritation

(5%, $n = 82$), skin exfoliation (5%, $n = 81$), pruritus (4%, $n = 57$), pain of skin (3%, $n = 49$), and rash (3%, $n = 47$).

Galderma launched a cleansing face wash with 5% BPO in 2018, and this launch led to a sharp increase in AE reports. From 2018 to October 2021, there were 488 reported AE cases. Prior to 2018, Galderma did not have any over-the-counter products that contained BPO. The increase in AEs was expected due to routine surveillance.

DISCUSSION

A total of 558 AE reports were recorded by the Galderma Global Safety Database from 1992 to 2021. Considering that BPO was recommended by dermatology healthcare providers for use more than 13 million times as an OTC product in the US between 1989 and 2008 alone [5], the reporting rate of AE reports concerning the use of OTC topical acne drug products containing BPO appears to be well under 1% at approximately 0.014%.

One limitation to this study is that, due to the nature of OTC products, subjects may not have been under the care of a dermatologist who may have recognized any AE and initiated a report.

Given this very low rate of AE reports, the risk–benefit of OTC topical acne drug products containing BPO is considered to be positive.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available due to the proprietary nature of the information contained in the reports. However, adverse event reports in the dataset that met the regulatory reporting criteria are accessible to the public through the FDA Adverse Event Reporting System (FAERS) database.

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